CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-420

CHEMISTRY REVIEW(S)

ANDA APPROVAL SUMMARY

AADA: 40-420

DRUG PRODUCT: Phenytoin Oral Suspension, USP

FIRM: Morton Grove Pharmaceuticals, Inc.

DOSAGE FORM: Oral Suspension, USP

STRENGTH: 125 mg/5 mL

CGMP STATEMENT/EIR UPDATE STATUS: Signed cGMP certifications provided on pages 2127 in original application. **EER is withhold dated 10/22/01.**

BIO STUDY: The bio-study conducted on the applicant's products (125 mg/5 ml) and Dilantin-125® were found acceptable by the Division of Bioequivalence on 7/26/01.

METHOD VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S): The drug substance and Drug product are both USP.

STABILITY - (ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?): Accelerated and room temperature stability data support the proposed 24 month expiration date. Containers used in the stability studies were identical to those described in the container section.

LABELING: Satisfactory as of 9/14/01

STERILIZATION VALIDATION (IF APPLICABLE): Not-applicable to this drug product.

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?): Exhibit batch (# A0253) used for stability and bio-studies were manufactured with bulk drug substance from [redacted]
The size for batch (# A0253) is [redacted]

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?): See above

PROPOSED PRODUCTION BATCH - (MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?): The proposed production batch size is [redacted]
[redacted] The manufacturing process described in the master production records is same as that described in the exhibit batch record.

1. CHEMISTRY REVIEW NO. 1 2. ANDA # **40420**

3. NAME AND ADDRESS OF APPLICANT
Morton Grove Pharmaceuticals, Inc.
6451 West Main Street
Morton Grove, IL 60053

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Dilantin-125
Innovator Company: Parke-Davis Division of Warner-Lambert
Patent Expiration Date: No unexpired patents or exclusivity for this drug product.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Phenytoin Oral Suspension, USP 125 mg/5 mL

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Submission date	**Submission type**
09/29/00	Original
2/2/01	Amendment

10. PHARMACOLOGICAL CATEGORY
Anticonvulsant

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

DMF number	DMF type	LOA(s) (page)
	III	
	III	
	III	
	IV	
	III	
	III	
	II	
	III	
	III	
	III	

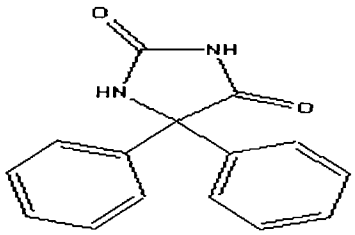
13. DOSAGE FORM
Suspension

14. POTENCY

Strength
125 mg/5 m

15. CHEMICAL NAME AND STRUCTURE

CAS number:	57-41-0
Molecular Weight:	252.27
Chemical Name:	2,4-Imidazolidinedione, 5,5-diphenyl-5,5-diphenylhydantoin



Structure:

16. RECORDS AND REPORTS
N/A

17. COMMENTS

[

]

18. CONCLUSIONS AND RECOMMENDATIONS
Not Approvable (MINOR)

19. REVIEWER:
Yanping Pan

DATE COMPLETED:
4/13/01

Redacted 29

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1. CHEMISTRY REVIEW NO. 2 2. ANDA # **40420**

3. NAME AND ADDRESS OF APPLICANT
Morton Grove Pharmaceuticals, Inc.
6451 West Main Street
Morton Grove, IL 60053

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Dilantin-125
Innovator Company: Parke-Davis Division of Warner-Lambert
Patent Expiration Date: No unexpired patents or exclusivity for this drug product.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Phenytoin Oral Suspension, USP 125 mg/5 mL

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Submission date	Submission type
09/29/00	Original
2/2/01	Amendment
9/20/01	Minor Amendment

10. PHARMACOLOGICAL CATEGORY
Anticonvulsant

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

APPEARS THIS WAY
ON ORIGINAL

DMF number	DMF type	LOA(s) (page)
[redacted]	III	[redacted]
	III	
	III	
	IV	
	III	
	III	
	II	
	III	
	III	
	III	

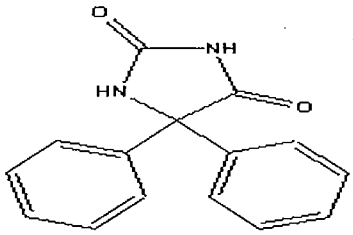
13. DOSAGE FORM
Suspension

14. POTENCY

Strength
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE

CAS number:	57-41-0
Molecular Weight:	252.27
Chemical Name:	2,4-Imidazolidinedione, 5,5-diphenyl-5,5-diphenylhydantoin



Structure:

16. RECORDS AND REPORTS
N/A

17. COMMENTS

[redacted]

This review covers Amendment September 20, 2001

Redacted 30

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1. CHEMISTRY REVIEW NO. **3** 2. ANDA # **40420**

3. NAME AND ADDRESS OF APPLICANT
Morton Grove Pharmaceuticals, Inc.
6451 West Main Street
Morton Grove, IL 60053

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Dilantin-125
Innovator Company: Parke-Davis Division of Warner-Lambert
Patent Expiration Date: No unexpired patents or exclusivity for this drug product.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Phenytoin Oral Suspension, USP 125 mg/5 mL

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Submission date	Submission type
09/29/00	Original
2/2/01	Amendment
9/20/01	Minor Amendment
2/22/02	Minor Amendment

10. PHARMACOLOGICAL CATEGORY
Anticonvulsant

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

APPEARS THIS WAY
ON ORIGINAL

DMF number	DMF type	LOA(s) (page)
[redacted]	III	[redacted]
	III	
	III	
	IV	
	III	
	III	
	II	
	III	
	III	
	III	

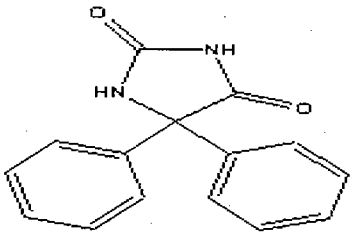
13. DOSAGE FORM
Suspension

14. POTENCY

Strength
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE

CAS number:	57-41-0
Molecular Weight:	252.27
Chemical Name:	2,4-Imidazolidinedione, 5,5-diphenyl-5,5-diphenylhydantoin



Structure:

16. RECORDS AND REPORTS
N/A

17. COMMENTS
EERs: **withhold (10/22/01)**
DMF (# —, status: adequate (2/20/01)
Labeling review: Approved (9/14/01)
Bio-review: Acceptable (7/26/01)
Micro review: N/A

This review covers Minor Amendment dated 2/22/02
#1 deficiency per review 2:
The specific gravity limit for finished product is not same as that for stability study. Please provide justification.

Response:

Based on the accrued stability data, MGP has revised the limits for specific gravity for the stability study to be consistent with limits for finished product. The limits have been tightened from ' [redacted] ' to " [redacted]

Comment per CR#3:

It is satisfactory.

#2 deficiency per review 2:

Please tighten your Sodium Benzoate specification for stability study.

Response:

Based on the discussion with OGD reviewer, the specification for Sodium Benzoate as currently established is acceptable to the FDA.

Comment Per CR#3:

It is satisfactory.

#3 deficiency per review 2:

We noticed that the following specifications listed in your Finished Product Quality Control Test Record and in your Certificate of Analysis are not consistent. Please clarify.

- *Sodium Benzoate*
- *Viscosity*
- *pH*
- *Specific gravity*
- *Individual known, individual unknown and total impurities*
- *Microbial limits*

Response:

MGP's Finished Product Quality Control Test Record (MGP Form 167) is the official document for released or rejected finished product. The Certificate of Analysis (MGP form 166) is a summary sheet prepared for MGP's customers and is shipped with the product. Thus, MGP Form 167 states release specifications, while MGP Form 166 summarizes stability specifications (per MGP Form 163). All tests included in Form 167 are included on Form 166 except for assay for degradants/impurities (individual and total).

Comment per CR#3:

It is satisfactory.

#4 deficiency per review 2:

We continue believing that you should tighten specifications for individual known and individual unknown impurities in your release and during stability for the drug product to reflect your actual data.

Response:

The limits for individual known and unknown impurities in the stability of the drug product have been tightened and revised as follows:

Parameters	Stability specification	
	From	To
Degradant/impurities individual (known)	NMT —	NMT —
Degradant/impurities individual (unknown)	NMT —	NMT —

Comment per CR#3:

The revised limits for individual known and unknown impurities in release and the stability of the drug product are as follows:

Parameters	Release specification	Stability specification
Degradant/impurities individual (known)	NMT —	NMT —
Degradant/impurities individual (unknown)	NMT —	NMT —

For total impurity specification, please see #6 deficiency. It is acceptable.

#5 deficiency per review 2:

We noticed that you deleted Antimicrobial Effectiveness testing and Microbial Limits testing from finished product quality control test. Please clarify.

Response:

MGP has not decreased the microbial testing commitments for this product.

MGP submits that the Microbial Limit testing continues to be reported without any changes as indicated on page 9 of 9 of MGP Form 167, finished Product Quality Control Test Record (Attachment 3).

The Antimicrobial Effectiveness Testing has been the subject of Minor reporting changes. The Antimicrobial Effectiveness Testing will be reported on MGP Form 165, Antimicrobial Effectiveness Test Worksheet (Attachment 5), which is a batch record document.

Comment per CR#3:

It is satisfactory.

#6 deficiency per review 2:

Please tighten the following limits during stability study for your drug product to reflect actual data:

- *pH*
- *Total impurity*

Response:

The Limit for pH in the stability of the drug product has been tightened and revised from " [redacted] " to " [redacted] ".

The limits for total impurity in the release and stability of the drug product have been tightened and revised as follows:

Parameters	Release specification		Stability specification	
	From	To	From	To
Total impurities	NMT [redacted]	NMT [redacted]	NMT [redacted]	NMT [redacted]

Comment per CR#3:

It is satisfactory.

18. CONCLUSIONS AND RECOMMENDATIONS
Approval (Pending Satisfactory EER)

19. REVIEWER: Yanping Pan

DATE COMPLETED: 3/7/02

APPEARS THIS WAY
ON ORIGINAL

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